Us TOO® PROSTATE CANCER EDUCATION & SUPPORT

HOT SHEET

NOVEMBER 2004

LOWER INCOME PATIENTS LESS INFORMED ABOUT CANCER TREATMENTS

Prostate cancer patients from lower income brackets are less informed about their treatment options, less likely to seek a second opinion and more often unhappy with their treatment decision than patients from higher income brackets, according to a new study presented October 3, 2004, at the American Society for Therapeutic Radiology and Oncology's 46th Annual Meeting in Atlanta.

There are several different treatment options available to prostate cancer patients, including radiation therapy, surgery and hormone therapy. Because of this, patients face difficult decisions in deciding the best treatment for their cancer and lifestyle. Various factors, such as income, can impact how much treatment information a patient receives and can influence the patient's decision. Researchers in this study sought to evaluate how income alone affects a patient's treatment decision and satisfaction afterwards.

In 2003, researchers conducted an online survey of 4,587 prostate cancer patients and their caregivers. Of them, 87 percent were prostate cancer patients, 72 percent of whom had been diagnosed within the past two years. The majority of patients were Caucasian - 93 percent - and 66 percent had completed college.

Researchers found patients with higher incomes felt better informed about the disease, were more likely to seek a second

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CURCUMIN ALTERS PCA CELL MOTILITY AND MICROFILAMENT ORGANIZATION

"Curcumin is a dietary phytochemical associated with anti-tumorigenic effects, but the mechanisms by which it inhibits cancer cell growth and metastasis are not completely understood. For example, little information is available regarding the effects of curcumin on cytoskeletal organization and function," scientists in the United States advise.

"In this study, time-lapse video and immunofluorescence labeling methods were used to demonstrate that curcumin significantly alters microfilament organization and cell motility in PC-3 and LNCaP human prostate cancer cells in vitro," said J. Holy and colleagues, University of Minnesota, School of Medicine.

"Curcumin rapidly arrests cell movements and subsequently alters cell shape in the highly motile PC-3 cell line, but has a less noticeable effect on the relatively immobile LNCaP cell line. Stress fibers are augmented, and the overall quantity of f-actin appears to increase in both types of cells following curcumin treatment.

"Cytochalasin B (CB) disrupts microfilament organization in both cell lines, and causes vigorous membrane blebbing in PC-3 cells, but not LNCaP cells. Pre-treatment of cells with curcumin suppresses changes in microfilament organization caused by CB, and blocks

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RESEARCHERS UNCOVER A KEY DRIVER BEHIND PROGRESSION OF PCA

Scientists at Fred Hutchinson Cancer Research Center have uncovered a key driver behind the progression of prostate cancer, a discovery that the researchers believe could spawn new treatments to prevent the cancer's spread and extend survival.

The study, conducted by Valeri Vasioukhin, PhD, and colleagues in Fred Hutchinson's human biology division, in collaboration with researchers at Vanderbilt University, appears as the cover story of the August 24, 2004 issue of Cancer Cell.

The work focused on a protein called hepsin, which has been found in high levels in human prostate and ovarian tumors. In the current study, Vasioukhin and colleagues asked what would happen if hepsin was overproduced in mice that had nonprogressing forms of prostate cancer. They found that hepsin caused prostate-tumor cells to lose their grip from the surrounding tissue and to spread from the prostate to bone, lung, and liver.

Hepsin's specific role in cancer progression, as well as the fact that it is a type of enzyme known as a protease, makes it a highly promising drug target, said Vasioukhin, an assistant member of Fred Hutchinson's human biology division.

"Because hepsin is a protease - and

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US TOO PUBLICATIONS

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MEN WITH ADVANCED, INCURABLE PCA CAN BENEFIT FROM DOCETAXEL-CHEMOTHERAPY

An international study led by a Canadian researcher shows that men with advanced, incurable prostate cancer can survive an average of three months longer and face less symptoms when offered a new treatment for prostate cancer.

Published in tomorrow's issue of The New England Journal of Medicine, the study involved 24 countries and over two years tracked more than 1,000 patients with advanced hormone-refractory prostate cancer. The patients were randomly divided into three groups, with one group receiving the standard chemotherapy (mitoxantrone), while the other two groups received docetaxel either every three weeks or weekly. All three groups received low daily doses of prednisone. Researchers looked at several outcome measures - survival, pain relief, improved quality of life, and the amount of PSA in the patients' blood, which indicates the amount of cancer present in the body. In all these measures, men who received docetaxel administered every three weeks did better than those who received mitoxantrone, and it improved survival by an average of three months. There was no significant difference in survival between those patients receiving docetaxel weekly and those receiving mitoxantrone.

"The new treatment of docetaxel results in many patients feeling better and living a few months longer," said Dr. Ian Tannock, the study's lead author and medical oncologist at Princess Margaret Hospital, senior scientist with Ontario Cancer Institute, and professor with the University of Toronto. "As a result, we are recommending docetaxel every three weeks with daily prednisone as the new standard of treatment for many patients with advanced hormone-refractory prostate cancer."

IMPOTENCE DRUGS COULD BE COVERED UNDER NEW MEDICARE PLAN

Impotence drugs such as Viagra, Cialis and Levitra - and possibly a libido-enhancing drug for women - could all be covered under the new Medicare prescription drug plan.

U.S. Pharmacopeia, the independent drug standards agency hired by Medicare to help decide what drugs to cover, has included "impotence agents" on its draft list of recommended drug classes for the benefit, which begins in 2006.

Critics say the drugs' possible inclusion, while popular among seniors, isn't medically warranted and will increase the new drug benefit's cost, which is projected to reach $534 billion by 2014.

"If you have a certain amount of money that you want to spend on health care for the elderly, how much of a priority is covering these types of pharmaceuticals as opposed to other therapeutic interventions? I think most experts would put these types of (drugs) fairly far down on the priority list," said Robert Reischauer, president of the Urban Institute, a Washington research group.

It's unclear what the demand for impotence drugs would be among the 65-and-older population if available from Medicare for a modest co-payment rather than the current cost of $8 to $10 a pill. Impotence drugs for men are a $1.3 billion U.S. market today and sales are projected to grow to between $3 billion and $3.5 billion by 2011.

Impotence-drug advertising today targets male baby boomers in their 40s and 50s. By the time they reach Medicare eligibility at age 65, they are likely to be regular users. according to studies, which have found that prior sexual interest and activity levels predict one's sex life after 60. Researchers at Duke University found that 80 percent of men in their late 60s remain interested in sex and that 1 in 4 men aged 78 and older is still sexually active.

A drug to increase sexual desire in post-menopausal women may also be covered under Medicare if the Food and Drug Administration approves the sale of a female testosterone patch developed by Procter & Gamble and Watson Pharmaceuticals Inc. Roughly 24 million of Medicare's 42 million enrollees are women.

"It is a problem that requires pharmacological intervention for many couples and for many individuals, so (the patch) should definitely be available," through Medicare, said Dr. Gloria Bachmann, the director of the Women's Health Institute at the UMDNJ-Robert Wood Johnson Medical School in New Brunswick, N.J.

Medicare officials say it's too soon to say what drugs will be covered under the new benefit. U.S. Pharmacopeia has until Dec. 31 to submit its final draft of recommended drug classes for the Medicare plan. Medicare is expected to finalize the list early in 2005.

Omitting coverage for impotence drugs would save money for cost-pressed Medicare, whose enrollee population is projected to grow to about 61 million by 2020. But impotence is a recognized medical condition and drugs to treat it are covered not only by Medicaid, but also by the Veterans Administration, the Federal Employees Health Benefit Plan and many private plans.

Private and public plans typically require that a physician determine that impotence drugs are medically necessary. Some plans require prior authorization before payment is made. Others restrict the number of prescriptions they'll cover over a certain time period. Some don't cover the drugs at all. Often, coverage is "decided on a case-by-case basis depending your health plan and your employer," said Mohit Ghose, a spokesman for America's Health Insurance Plans, the leading trade group for health insurers.

While impotence medications aren't essential for survival, doctors say they're therapeutically necessary in certain medical situations. The main causes of impotence are physiological, not psychological, said Dr. Michael Fleming, a family physician in Shreveport, La., and president of the American Association of Family Physicians. For instance, erectile dysfunction often occurs in patients with diabetes or prostate cancer.

"That's not something that a patient can help," Fleming said. "It's caused by a disease and these drugs effectively treat it. So for that patient this is not a lifestyle drug. It's something very important to him."

Fleming said he prescribes impotence drugs mostly to patients between 50 and 65 years old, but less frequently to older patients. For that reason, he and others don't foresee a major run on the drugs by sex-crazed seniors.

But if Medicare foots the bill, doctors could prescribe impotence drugs to improve sexual performance rather than to treat erectile dysfunction. Drug-industry consultant Dr. David J. Goldstein of Indianapolis compared it to doctors who cave in to patients' demands for antibiotics to treat their colds, even though antibiotics treat infections rather than the viruses that cause colds.

Doctors who refuse such requests, Goldstein said, risk losing patients to physicians willing to bend the rules. "Doctors are under pressure to prescribe drugs that patients read about in order to maintain the relationship with that patient," Goldstein said. "It's the practice of medicine versus the theory of medicine."

HOT FLASHES IN MEN : MAYO CLINIC STUDY DETAILS TREATMENT WITH A NEW ANTIDEPRESSANT MEDICATION

A new antidepressant medication is an effective treatment for diminishing hot flashes in men who are receiving hormone therapy for prostate cancer, Mayo Clinic researchers report in the October issue of Mayo Clinic Proceedings.

The five-week study followed 18 men who completed the therapy, illustrating that their hot flashes decreased from 6.2 per day to 2.5 per day. Hot flash scores, the frequency multiplied by the severity, decreased in the same period from 10.6 per day to 3 per day.

"Newer antidepressants have been proven effective in reducing hot flashes in women but have not been studied in men," says Charles Loprinzi, M.D., Mayo Clinic Division of Medical Oncology and the lead author of the study. "Although hot flashes in men with prostate cancer are well documented, their treatment has not received as much attention." Hormonal treatments for male hot flashes have been studied, but there is a concern that they may affect prostate cancer growth and/or cause significant side effects.

The study looked at men receiving androgen ablation therapy, also known as hormonal deprivation therapy, which is a well-established treatment for various stages of prostate cancer. The antidepressant used, paroxetine, has been used to treat mental depression, obsessive-compulsive disorder, panic disorder, generalized anxiety disorder and social anxiety disorder, among others. A placebo-controlled trial had previously demonstrated that paroxetine reduced hot flashes in women.

The study was conducted between August 2001 and October 2003. Men eligible for the study had to have a history of prostate cancer for which they were receiving androgen ablation therapy.

NANOPARTICLES FOR EARLY DETECTION OF TUMORS

Cancer treatment relies heavily on the early detection of tumors. Researchers at Emory University and Georgia Institute of Technology (GIT) developed a new method for targeting and imaging cancerous tumors in vivo ."We want to use this technology for early cancer detection, so that we can detect a very small [millimeter-sized] tumor," says Xiaohu Gao, PhD, post-doctorate fellow, Coulter Dept. of Biomedical Engineering, Emory University and GIT, Atlanta.

The researchers injected mice with nanoparticles called quantum dots, which were chemically linked to monoclonal antibodies and used to detect the prostate-specific membrane antigen on the cell surface of the tumors in the living mice.

"Initially, this will allow us to limit cancer growth in living animal models at a higher sensitivity," says Shuming Nie, PhD, director of cancer nanotechnology, Winship Cancer Institute. "It probably can be used to monitor the treatment of therapeutic drugs and it is possible that there is going to be something in the future for human patient studies. We still need to do a more careful study on the toxicity, and how the quantum dots get metabolized and secreted," he says.

Nie and his group plan to continue their research by creating multicolored quantum dots with different intensities that will allow researchers to monitor multiple parameters Drug Discovery and Development provides the pharmaceutical and biotech research community with the latest developments in the technology, tools and services used in drug discovery research and development.

CANCER TREATMENT LEADS TO IMPAIRMENTS

Treatment for prostate cancer leads to significant 5-year declines in sexual and urinary function, according to a new study. However, general and other specific health-related quality-of-life factors, such as bowel function, are not affected.

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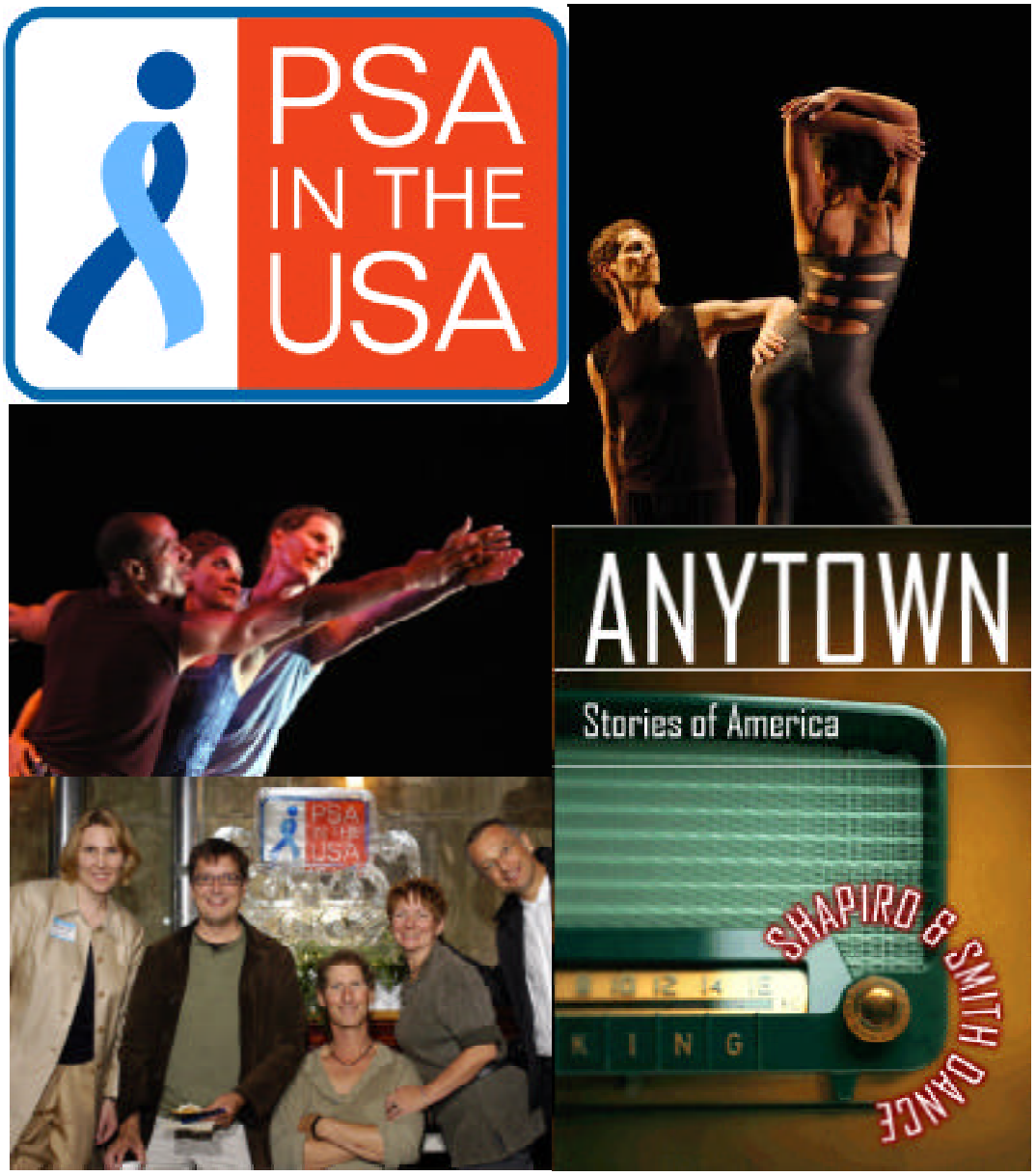
SHAPIRO & SMITH'S *ANYTOWN* PERFORMANCE PROMOTES PROSTATE CANCER AWARENESS & PATIENT SUPPORT

The "PSA in the U.S.A." campaign - a partnership between Us TOO and the national tour of Danial Shapiro and Joanie Smith's "*ANYTOWN: Stories of America,"* – kicked off in August with a benefit show in Minneapolis.

The *ANYTOWN* show was created by Mr. Shapiro who was diagnosed with prostate cancer at age 44 in October 2002. The awareness campaign seeks to reach 1 million men over the course of a 5-7 year national tour. "*ANYTOWN"* dances to the music of Rock & Roll Hall of Famer Bruce Springsteen, his wife, Patti Scialfa, and Estreeter Soozie Tyrell – who is Ms. Smith's sister. The mission of the partnership is to tell men that despite the fact that prostate cancer is the second leading cause of cancer death in men, it is nearly 100 percent survivable if detected early.



"My diagnosis forced Joanie and me to focus on the priorities of getting well, but also guided our hand to the work we felt compelled to do. Since we had long dreamt of dancing with the music of Soozie, Patti and Bruce, our course was set. "ANYTOWN marks not only the most exciting collaboration of our careers, but also celebrates survival on a very personal level," says Joanie. "Getting out of bed and going back into the studio has given extra purpose to our waking moments and shown us that our strength as artists has helped us in this fight for our lives." Danial says, "At the heart of ANYTOWN is the importance of family—the actual family you are born into and the family you create. Dancing to Soozie, Bruce and Patti's music makes ANYTOWN the thrill of a lifetime."

The "PSA in the U.S.A." campaign will benefit Us TOO. "I met people from Us TOO at a Prostate Cancer conference in September 2003. We talked a while and they remarked on my having written – 'Yes – Me Too' on my name badge as a response to all the inquisitive looks from the mostly older men. We discussed the need for consciousnesses raising among men my age whose Dad's have had prostate cancer. We figured that maybe I could become a 'poster boy' for my generation!" Through receptions, following performances, "PSA in the U.S.A." will provide fun, music, a dessert smorgasbord, literature and free prostate cancer early detection PSA blood testing. American Medical Systems sponsored the reception in Minneapolis.

More ANYTOWN information can be found at: http://www.shapiroandsmithdance.org/psa_in_the_usa.html

IMPAIRMENTS

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These findings come from the first prospective comparative study examining differences between normal aging and the effects of prostate cancer treatment, published in the November 1, 2004, issue of Cancer.

Generally a very slowly progressing cancer, early prostate cancer is treated aggressively with radiation or radical prostatectomy. However, only one study, on surgical removal of the prostate, has proved therapeutic benefit of treatment compared with observation. Meanwhile, treatments themselves are often associated with significant adverse effects, such as impotence and urinary incontinence. To date, studies have been unable to distinguish between the normal effects of aging and the adverse effects of treatment, confounding any informed decision making about which treatment to use.

In the first prospective comparative quality-of-life analysis of prostate cancer patients and matched healthy subjects, Richard M. Hoffman, MD, MPH, of the New Mexico Veterans Administration Health Care System in Albuquerque, and his colleagues compared the effects of cancer treatment vs. aging in men over a 5-year period.

They found even healthy subjects reported declines in sexual function over the 5 years. But the decline among patients treated for prostate cancer over that same time period was much greater, and was accompanied by significant declines in urinary function as well. General and other specific health-related quality-of-life factors were not affected by cancer.

The authors concluded, "Declines in urinary and sexual functional domains after diagnosis and treatment of localized cancer far exceeded any effects from aging, particularly for men undergoing radical prostatectomy."

GLASS OF RED WINE A DAY MAY KEEP PCA AWAY

Drinking a glass of red wine a day may cut a man's risk of prostate cancer in half, and the protective effect appears to be strongest against the most aggressive forms of the disease, according to a new study led by investigators at Fred Hutchinson Cancer Research Center.

The findings, by Janet L. Stanford, PhD, and colleagues in Hutchinson's Public Health Sciences Division, appear online in the International Journal of Cancer.

"We found that men who consumed four or more glasses of red wine per week reduced their risk of prostate cancer by 50%," Stanford said. "Among men who consumed four or more 4-ounce glasses of red wine per week, we saw about a 60% lower incidence of the more aggressive types of prostate cancer," said Stanford, senior author of the study. "The more clinically aggressive prostate cancer is where the strongest reduction in risk was observed."

Stanford and colleagues found no significant effects - positive nor negative - associated with the consumption of beer or hard liquor and no consistent risk reduction with white wine, which suggests that there must be a beneficial compound in red wine that other types of alcohol lack. That compound, Stanford and colleagues believe, may be an antioxidant called resveratrol, which is abundant in the skins of red grapes but much less so in the skins of white grapes. The compound is also found in peanuts and raspberries and is available as a dietary supplement, which has been suggested to protect against cardiovascular disease.

Laboratory studies indicate that resveratrol influences a variety of biological pathways that are important in cancer development. For example:

1) As an antioxidant, it helps sweep dangerous, cancer-causing free radicals from the body.

2) As a potent anti-inflammatory agent, it blocks certain enzymes that promote tumor development.

3) The compound also reduces cell proliferation, curtailing the number of cell divisions that could lead to cancer or the continued growth of cancer cells.

4) It also enhances apoptosis, or programmed cell death, which helps rid the body of cancerous cells.

5) It may act as an estrogen, reducing levels of circulating male hormones such as testosterone that fuel the growth of prostate cancer.

While the researchers found that the risk of prostate cancer decreased 6% for every glass of red wine consumed per week, Stanford was quick to point out that research shows the law of diminishing returns comes into play when consumption increases beyond moderation. "From a public-health standpoint, it's difficult to recommend any alcohol consumption given the risks associated with heavy consumption, from increased overall cancer risk to accidental injury and social problems. But for men who already are consuming alcohol, I think the results of this study suggest that modest consumption of red wine - four to eight 4-ounce drinks per week - is the level at which you might receive benefit. Clearly other studies show that more than that may have adverse effects on health."

For the study, the researchers interviewed 753 newly diagnosed Seattle-area prostate cancer patients as well as 703 healthy controls who served as a comparison group. Detailed information about tumor aggressiveness (such as tumor grade and disease stage) was obtained through the National Cancer Institute's Seattle-Puget Sound Surveillance, Epidemiology and End Results cancer registry.

"Even though this study is based on relatively small numbers, the results are very intriguing and suggest that the potential beneficial effect of red wine and resveratrol - if indeed resveratrol is the active chemopreventive agent involved - would be very important, because it's the more aggressive forms of prostate cancer than are most important to prevent," she said.

A particular strength of the study, Stanford said, is that the participants were relatively young, ranging in age from 40-64, and the majority were under 60.

"By focusing on men under age 65, whose incidence of prostate cancer is much lower than that of older men, we can tease out the effect of a particular environmental exposure on cancer risk, such as wine consumption, more easily than if we were looking at men across the entire age range," she said. This is particularly true when studying complex diseases such as prostate cancer in which numerous genetic and environmental factors are thought to play a role over an individual's lifetime.

Another strength of the study is that in addition to being surveyed about lifetime alcohol consumption, participants were asked about a variety of other risk factors for prostate cancer, such as diet, family

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RED WINE

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history of cancer, screening for prostate cancer and tobacco use, all of which were taken into account and adjusted for when analyzing the data.

While the majority of studies to date have assessed the effects of overall alcohol use on prostate cancer risk, fewer studies have attempted to compare the effects of wine vs. beer vs. hard liquor, and only one previous study has compared the impact of red vs. white wine on prostate cancer risk, said Stanford, also a professor of epidemiology at the University of Washington School of Public Health and Community Medicine.

The previous study, the Netherlands Cohort Study, evaluated prostate cancer risk in relation to white and red wine consumption. Increased risks were found in men who consumed "white and fortified wines," but not red wine, as compared to nondrinkers, although there was not a consistent trend in risks with levels of intake.

Interestingly, among men who consumed 15 or more g of red wine per day (about 1 1/2 glasses per day), there was an overall 18% reduction in risk and a 16% lower risk of advanced-stage prostate cancers. The Netherlands Cohort Study was initiated in 1986 and collected information by self-administered mailed questionnaires that asked about alcohol consumption during the prior year only. Thus, the Netherlands Cohort Study results only reflect associations with recent wine consumption, as investigators were unable to examine lifetime intake as was done in the current Fred Hutchinson study.

"One of the reasons we wanted to do this study is because overall, most of the scientific literature - around 17 studies to date - haven't shown a consistent relationship between alcohol consumption and prostate cancer," Stanford said. "Some have shown an increase, some a decrease, and most no association whatsoever. Part of the problem, we believe, is that few of the studies have attempted to sort out the effects of different types of alcohol intake over a man's lifetime."

FRESH GRAPES LINKED TO CANCER PREVENTION

Two and a half cups of fresh grapes a week may cut the risk of some cancers in half, according to the results of a new study by the Fred Hutchinson Cancer Research Center.

The latest research on a compound called resveratrol is good news for people who like fresh grapes. Resveratrol is a powerful antioxidant found in the skins of fresh grapes and has been linked to lowering the risk of prostate cancer in the new study.

Consumers can get the necessary amount of resveratrol by eating fresh grapes of any color. Because red wine is fermented with the skins, red wine contains resveratrol and the study linked the reduced prostate risk to the consumption of red wine, reporting that four or more glasses of red wine per week may cut the risk of prostate cancer in half. The findings appear in the current issue of the International Journal of Cancer.

But red wine is not the only source for the compound. "Fresh grapes have the same range of concentrations of resveratrol as red wines," says Dr. Le Creasy, who discovered resveratrol in grapes through his work at Cornell University in the early nineties and has researched it extensively ever since. "A pound of grapes per week provides the same amount of resveratrol as four glasses of red wine." One pound equals approximately two and a half cups of the fruit.

The study is the latest in a string of reports linking fresh grapes and grape compounds with disease prevention. In the July, 2004 publication Nature, it was reported that researchers at Harvard University found that resveratrol may contribute to increased longevity in the same way that caloric restriction does, by decreasing the development of fat cells and increasing the use of fat within existing cells. Resveratrol was also shown to prevent premature cell death. Further studies are underway.

Research has established that resveratrol and other antioxidants are found in the skins of red, green and blue-black grapes.

LOW DOSE RADIATION EVADES CANCER CELLS' PROTECTIVE "RADAR"

A new study shows that lower doses of radiation elude a damage detection "radar" in DNA and actually kill more cancer cells than high-dose radiation. With these findings, scientists believe they can design therapy to dismantle this "radar" sensor allowing more radiation to evade detection and destroy even greater numbers of cancer cells.

Researchers at the Johns Hopkins Kimmel Cancer Center tested the low-dose radiation strategy on cultured prostate and colon cancer cell lines and found that it killed up to twice as many cells as high-dose radiation. The extra lethality of the low-dose regimen was found to result from suppression of a protein, called ATM (ataxia telangiectasia mutated) which works like a radar to detect DNA damage and begin repair.

Theodore DeWeese, M.D., who led the study, speculates that cells hit with small amounts of radiation fail to switch on the ATM radar, which prevents an error-prone repair process. DeWeese, who will present his evidence at the annual meeting of the American Society for Therapeutic Radiology and Oncology on October 5 in Atlanta, explains.

"DNA repair is not foolproof - it can lead to mistakes or mutations that are passed down to other generations of cells," explains DeWeese, chairman of the Department of Radiation Oncology and Molecular Radiation Sciences at Johns Hopkins. "A dead cell is better than a mutant cell, so if the damage is mild, cells die instead of risking repair."

Higher doses of radiation cause extreme DNA damage and widespread cell death, so the ATM damage sensor is activated to preserve as many cells as possible, protecting, ironically, the cancer cells under target for destruction by the radiation.

While the low-dose regimen works in cultured cells, it has not proved successful in humans. This has lead to effort by Hopkins scientists to study ways to use viruses that can deliver ATM-blocking drugs to the cells. Tests in animals are expected to begin soon.

In the current study, colon and prostate cancer cells lines were treated with either high levels of radiation or small amounts spread over many days. Low-level radiation is approximately 10 times more powerful than normal exposure, while high doses are 1,000 times stronger. Approximately 35 percent of colon cancer cells survived low-dose radiation as compared to 60 percent receiving high-dose. In prostate cancer cell lines, half of the cells survived low-dose radiation, while 65 percent remained in higher doses.

In the low-dose group,ATM activation was reduced by 40 to 50 percent. The researchers proved ATM inactivation was the culprit since low-dose irradiated cells fared better after ATM was reactivated with chloroqine, best known as a treatment for malaria.

"Tricking cancer cells into ignoring the damage signals that appear on its radar could succeed in making radiation more effective in wiping out the disease," says DeWeese.

Collis, S. et al, "Low-Level Radiation-Induced DNA Damage Evades Early Cellular Response Mechanisms Leading to Increased Cell Death," ASTRO Proceedings, Abstract #2012.

SUNLIGHT EXPOSURE ASSOCIATED WITH REDUCED PROSTATE CANCER RISK

Study results from the United States associate sunlight exposure with reduced prostate cancer risk. "The possibility that exposure to sunlight reduces the risk of clinical prostate cancer has been strongly suggested by ecologic data. However, data on prostate cancer risk in relation to sunlight exposure in individuals are sparse," wrote G.G. Schwartz and colleagues.

"We analyzed data from the First National Health and Nutrition Examination Survey (NHANES 1) Epidemiologic Follow-up Study in order to test the hypothesis that residential sunlight exposure reduces the risk of prostate cancer."

"We identified 153 men with incident prostate cancer from a cohort of 3414 white men who completed the baseline interview and dermatologic examination in 1971-1975 and were followed up to 1992," reported the researchers.

Schwartz and coauthors noted, "We used Cox proportional hazards modeling to estimate relative risks (RR) and 95% confidence intervals (Cl) for measures of residential sunlight exposure, adjusting for age, family history of prostate cancer, and dietary intake of fat and calcium.

"Residence in the South at baseline (RR = 0.68, CI = 0.41-1.13), state of longest residence in the South (RR = 0.62, CI = 0.40-0.95), and high solar radiation in the state of birth (RR = 0.49, CI = 0.30-0.79) were associated with significant and substantial reductions in prostate cancer risk."

The authors concluded, "These data support the hypothesis that sunlight exposure reduces the risk of prostate cancer and have important implications for prostate cancer prevention."

Schwartz and colleagues published the results of their research in Journal of Steroid Biochemistry and Molecular Biology (Residential sunlight exposure is associated with a decreased risk of prostate cancer. J Steroid Biochem Mol Biol, 2004;89-90(1-5 Sp. Is):549-552).

HERBAL SUPPLEMENT MAY PREVENT PROSTATE CANCER

Columbia University Medical Center has launched the first clinical trial of a possible herbal preventative for prostate cancer. The Phase I study will determine whether Zyflamend(R), an herbal supplement commonly used as an anti-inflammatory, can prevent prostate cancer in patients with prostatic intraepithelial neoplasia (PIN).

PIN is a clinical precursor for prostate cancer. Without intervention, men diagnosed with PIN have a 50 to 70 percent likelihood of developing prostate cancer.Although there are tools that detect the early signs of prostate cancer, such as PIN or elevated prostate specific antigen (PSA) levels, there is no consensus as to the optimal therapy for these patients.

"Zyflamend has shown an ability, in vitro, to reduce prostate cancer cell proliferation by as much as 78 percent and to induce cancer cell death or apoptosis," saysAaron E. Katz, M.D., associate professor of urology at Columbia University College of Physicians and Surgeons, Director of the Center of Holistic Urology at Columbia University Medical Center and principal investigator of the study. "These results are exceptionally promising and have led us to initiate this clinical trial."

The herbal supplement, made by New Chapter, Inc., is composed of 10 herbs which inhibit the cyclooxygenase-2 (COX-2) inflammation pathway. Long-term chronic inflammation contributes to carcinogenesis in many organ systems (the origin of certain cancers); inhibiting this pathway appears to be key to preventing cancers like prostate and colon cancer.An herbal supplement such as this herbal supplement may inhibit this pathway without causing the adverse gastrointestinal side effects associated with the long-term use of other COX-2 inhibitors. The preparation of this herbal supplement differs from many herbal products in that it is not standardized to isolated chemicals. It delivers herbs in concentrated form, but the herbs retain their "food" status.

"We know more people are using herbal supplements as either their primary treatment or in tandem with their prescribed therapies, which is why it is important to study the safety and efficacy of herbal therapies," said Mark Blumenthal, founder and executive director of the non-profit American Botanical Council. "This study is an important step in a new direction for therapy in this area and holds much promise for millions of men with challenges in prostate health."

The Study
The Phase I study will evaluate the safety and tolerability of the herbal supplement in patients with PIN. Up to 48 men, between the ages of 40-75, will receive the herbal supplement three times a day for 18 months.

PIN and Prostate Cancer
PIN means that the top layer of cells or epithelial cells of the prostate are dividing more rapidly than normal epithelial cells. This development of pre-cancerous, abnormal tissue of the prostate gland puts men at high risk of developing prostate cancer.

Prostate cancer is a group of cancerous cells (a malignant tumor) that begins most often in the outer part of the prostate. It is the most common type of cancer (excluding skin cancer) diagnosed in American men. In 2003, an estimated 220,900 new cases of prostate cancer were diagnosed in the United States.

The Herbal Supplement
Zyflamend includes rosemary, turmeric, ginger, holy basil, green tea, hu zhang, Chinese goldthread, barberry, oregano, and Baikal skullcap.

LOW INCOME LESS INFORMED

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opinion and were generally happier with their treatment decision. According to the survey, 95 percent of patients who earned $120,000 or more said they felt informed about prostate cancer in general compared to 69 percent of patients earning less than $20,000 per year. Prior to treatment, 79 percent in the highest income bracket

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LOW INCOME LESS INFORMED

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sought a second opinion versus 47 percent in the lowest income range. Afterwards, 92 percent of patients making $120,000 or more said they would make the same treatment decision again compared to 77 percent in the $20,000 or less range.

"This study shows that prostate cancer patients in lower income brackets often lack information on treatment options, are less likely to receive a second opinion and are more often unhappy with their treatment afterwards," said Peter Grimm, D.O., lead author of the study and a radiation oncologist at the Seattle Prostate Institute, Swedish Medical Center in Seattle. "These results show that we must work harder to educate prostate cancer patients, particularly those in the lower income levels, about the disease and the treatment options available to cure it."

The study was funded and conducted in collaboration with Us TOO International, Inc., based in Downers Grove, Ill., and NexCura, Inc. of Seattle - two organizations interested in better understanding the unique educational needs of different patient populations diagnosed with prostate cancer.

CURCUMIN

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PC-3 membrane blebbing. At least some of the effects of curcumin appear to be mediated by protein kinase C (PKC), as treatment with the PKC inhibitor bisindolylmaleimide inhibits the ability of curcumin to block CB-induced membrane blebbing.

"These findings demonstrate that curcumin exerts significant effects on the actin cytoskeleton in prostate cancer cells, including altering microfilament organization and function. This is a novel observation that may represent an important mechanism by which curcumin functions as a chemopreventative agent, and as an inhibitor of angiogenesis and metastasis," scientists indicated.

Holy and colleagues published their study in Cell Motility and the Cytoskeleton (Curcumin inhibits cell motility and alters microfilament organization and function in prostate cancer cells. Cell Motility Cytoskel, 2004;58(4):253-268).]

KEY DRIVER OF PCA UNCOVERED

(continued from page 1)

proteases are relatively easy to inhibit - we think it will be possible to develop an inhibitor of hepsin that prevents metastasis," he said. "Previous research has demonstrated that hepsin is not critical for normal cells within the body and, therefore, hepsin inhibitors that are very specific would be unlikely to have significant side effects."

In collaboration with the laboratory of Julian Simon, PhD, of Fred Hutchinson's human biology and clinical research divisions, Vasioukhin's lab plans to search for small molecules that can inhibit hepsin.

"We are hoping that highly specific hepsin inhibitors can be used in the future to block or slow down the progression of prostate cancer from relatively harmless benign tumor to highly advanced metastatic disease."

The spread of cancer from its site of origin to another location in the body is called metastasis, a condition that can dramatically reduce a patient's chances for survival. The majority of prostate cancers are diagnosed while the disease is still confined to the prostate, a stage at which 5-year survival rates are nearly 100%. In contrast, when the disease has spread to distant parts of the body - commonly to the bone - only about a third of patients survive 5 years.

While doctors have dramatically improved survival rates for prostate cancer through earlier diagnosis, there remains a need for effective therapies for men whose disease is advanced, said Pete Nelson, MD, a human biology division investigator and a physician who treats prostate-cancer patients at the Seattle (Washington) Cancer CareAlliance.

"If hepsin indeed drives metastasis in human prostate cancer and if inhibitors of hepsin can be identified, it could offer new options for patients whose disease has spread," he said. "Alternatively, hepsin activity could be exploited to activate prodrugs (precursors of chemotherapeutic drugs that are toxic to cells) locally in the tumor environment where the protease is produced at high levels. This approach could spare normal tissues that produce the enzyme at low levels."

Hepsin is a member of a large family of enzymes called proteases, which are found in all animals. Some proteases play an important role in ensuring that cells are organized correctly within a tissue or organ. For example, cells that can give rise to prostate cancer must adhere to a scaffold-like structures, called basement membranes, that keep distinct layers of cells separated from one another.

To examine the consequences of excess amounts of hepsin, Vasioukhin's group developed a strain of mice that produced elevated amounts of hepsin in the prostate gland. The mice with elevated hepsin levels had defects in the basement membrane that separates different populations of cells. This finding was interesting because disorganization and disruption of the basement membrane is a mandatory step that occurs in early phases of metastasis.

Next, the researchers bred this mouse with a type of mouse that develops a form of prostate cancer that does not metastasize in order to generate cancer-susceptible mice that overproduce hepsin. They found that these mice developed more highly advanced prostate tumors and metastases in the liver, lung, and bone. These data provide strong evidence that hepsin promotes prostate-cancer progression and metastasis.

Vasioukhin said that hepsin is not normally produced in the mouse prostate. Hepsin overproduction was not observed in other mouse models of prostate cancer.

"One simplified way to explain our observations in mice is that overproduction of hepsin is what's necessary to drive prostate cancer metastasis to the bone," he said.

Although the absence of hepsin may prevent metastasis, Vasioukhin said that studies from human cancers suggest that very high levels might also prevent cancer from spreading.

"There have been controversial results about hepsin levels in human cancer," he said. "It may be that the change from very low levels to elevated levels of hepsin will promote metastasis. But in a few cases when the levels are too high, it may cause enough disruption to the cell's gripping abilities so that they can't form new attachments at sites in the body distant from the original tumor."

In addition to searching for inhibitors of hepsin, Vasioukhin's lab also plans to study mechanisms of hepsin function in prostate-cancer metastasis. Specifically, the researchers will try to determine how hepsin causes disorganization of the basement membrane.